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Bucharest, December 20th, 2023

TO: MINISTRY OF HEALTH

IN ATT: PROF. DR. ALEXANDRU RAFILA, MINISTER OF HEALTH

SUBJECT: REVISION OF THE EUROPEAN UNION PHARMACEUTICAL LEGISLATION

Dear Minister Rafila,

The current review process on the EU level of the pharmaceutical package is a **'once-in-a-generation' opportunity to ensure that Europe remains at the forefront of medical innovation, bringing the best care to patients**. The policy choices will have lasting impact over the coming decades and determine whether Europe can leverage the coming new wave of treatments being discovered or if the policies voted now will hamper important innovations for patients and weaken Europe's competitiveness and strategic autonomy.

AmCham Romania welcomes changes to the regulatory framework but is concerned by those which will raise challenges on the incentives' framework, our control over research and medicines, alongside disproportionate shortage, and environmental requirements.

Since Romania will also have to deliver a position on this matter, AmCham Romania's recommendations for a European Union Pharmaceutical Legislation that focuses on increasing patient access to medicines across Europe while strengthening the competitiveness of Europe's pharmaceutical sector are the following:

- Reinforce, rather than undermine the current Intellectual Property (IP) and incentives framework of Regulatory Data Protection (RDP) and Orphan Market Exclusivity (OME) and make it predictable to ensure EU competitiveness. As a minimum, bring RDP and OME back to their current baselines.
- Delink IP incentives from access/continuous supply and use the European Access Hurdles Portal[1] to develop a shared understanding of local access barriers and collaboratively work on more holistic solutions.
- Ensure the Unmet Medical Needs (UMN) definition is patient-centered and more inclusive of chronically debilitating diseases and medicines that significantly improve quality of life. The incentive should be more meaningful and include follow-on indications.
- Optimize the regulatory framework by shortening accelerated assessments and decision timelines and ensuring maximum use of expedited pathways to swiftly bring innovative medicines to patients.
- Ensure the involvement / consent of Marketing Authorization Holders (MAH) when introducing changes to product information or for repurposing of a medicine considering their expertise but also implications on liability, pharmacovigilance, supply and access.

[1] https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf

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- Make the framework for mechanism of action Pediatric Investigation Plans more robust with guardrails (e.g. applicable once per active substance) to ensure this obligation is manageable, considers therapeutic area expertise and is adequately rewarded (e.g. 12-month Supplementary Protection Certificate extension).
- Establish a list of critical medicines/shortages following clear and objective criteria, based on risk (e.g. availability of alternatives) and in collaboration with all supply chain stakeholders. Shortage Prevention / Mitigation Plans and additional corrective measures should also be based on risk and dialogue reflecting the *shared* responsibility of the various stakeholders to ensure continued patient access.
- Accelerate the harmonized EU roll-out of electronic-Patient Information Leaflets (e-PIL). Consider a stepwise implementation focusing on medicines administered by Healthcare Professionals.
- Align Environmental Risk Assessment provisions with the EU Parliament's resolution (2020)[2], suggesting that Marketing Authorizations (MAs) should not be refused *solely* on environmental grounds.

Through its Healthcare Committee, AmCham Romania is committed to **working with all Romanian stakeholders for a position at EU level that is consistent with our goal of achieving a healthier future for Romania and Europe**. The global pandemic showed that we need to increase investments in health to reflect the value we place on it as a society. Europe's research and industrial base is eroding with only 22% of global new treatments originating in Europe – almost half come from the US and competition from other regions is rising, particularly for advanced therapies[3]. In the addendum to this letter, we list a more comprehensive argumentation on the reasoning Romanian authorities should have in mind when putting together a position for this package at EU level.

Hoping for a constructive and transparent collaboration, we reiterate our full openness and willingness to support your efforts, through the expertise of the AmCham Romania Healthcare Committee members, and we assure you of our high consideration.

Best regards,

Vlad Boeriu
President
AmCham Healthcare Committee

[2] https://www.europarl.europa.eu/doceo/document/B-9-2020-0242_EN.html
[3] The Pharmaceutical Industry in Figures, Key data 2021, Pharmaprojects & SCRIP, March 2021

ADDENDUM

Incentives to innovate in Europe and unlock tomorrow's cures for patients

To attract continued investments in more complex areas of Unmet Medical Need (UMN) and ensure that medical innovation takes place in Europe and can be accessed much faster by European patients, the pharmaceutical package should **reinforce, not undermine the current IP and incentives framework**. Some proposals risk eroding the EU's industrial and research base to more competitive regions, ultimately delaying EU patients' access to cutting-edge science and innovation.

A strong patent system (incl. Supplementary Protection Certificates and Pediatric Extensions) and robust Regulatory Data Protection (RDP) are **fundamental for attracting investment in high-risk and lengthy R&D processes** for innovative medicines. Unlike in other industries, around half of the standard 20-year patent term is spent on rigorous clinical trials to demonstrate the safety / efficacy of a medicine before it can be made available to patients[4]. This means that in some cases (e.g. longer development timelines for complex innovations), RDP may be the only effective incentive to drive research and development of an innovative medicine[5].

Lowering baseline incentives for innovation

We are therefore **concerned by proposals to reduce RDP from 8 to 6 years and Orphan Market Exclusivity (OME) down to 9 years**. Together with uncertain and complex exclusivity modulations, this will undermine investments in the development of transformational therapies and as a result **adversely impact access/affordability objectives**. Weaker incentives may prevent a new product, indication and/or formulation from being developed (or mean that it is developed outside Europe), thereby undermining the pipeline of off-patent medicines in the long term[6]. It will impact the attractiveness to partner with the SMEs that cannot always adequately protect their assets through patents and rely on RDP. Weaker incentives might also lead to higher prices, given that industry will have a shorter time frame to recoup these high-risk investments in clinical development.

This measure will equally pose at risk the **EU's global competitiveness** and its ability to attract global investments, in an environment where Europe is already losing ground. Today only 22% of global new treatments originate in Europe (almost half come from the US) and competition from other regions is rising[7]. Of the total R&D investments made in the US, Europe, China and Japan, only 31% of this occurs in Europe (down from 41% in 2001). For advanced cell and gene therapies, clinical trial activity is twice as high in the US and almost three times as high in China than in Europe, and the gap is growing[8]. Regarding clinical trials

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[4] Copenhagen Economics, 2018

[5] RDP is essential for approximately 1/3rd of innovative medicines, notably for treatments for complex diseases and advanced therapies, with a long and/or difficult development programs e.g. neurodegenerative diseases etc. EFPIA Pipeline Review 2022

[6] Several factors influence generic/biosimilar launches: 1) Originator presence i.e. they were launched in +90% of cases, where the originator was already present; 2) Market size: smaller markets generally have few generic/biosimilar launches and the delay to launch from loss of market protection tends to be longer than in larger markets. Protection expiry and Journey into the market - IQVIA, Sept 2022.

[7] The Pharmaceutical Industry in Figures, Key data 2021, Pharmaprojects & SCRIP, March 2021

[8] Factors affecting the location of pharmaceutical investments, CRA Nov 2022

activity, Europe accounted for 19.3% of the global share in 2020 (down from a 25% average over the last 10 years). This **erosion will ultimately delay EU patient access** to innovation and in the longer term to generic medicines. Within that context, EU leaders in March 2023 called on the co-legislators to improve access but also strengthen incentives for innovation.

Since exclusivity is an important aspect for R&D investment decisions and business planning, the incentives system should be based on **clear and predictable criteria, which are attainable fairly**. Theoretically, the proposal gives the impression that, when all incentives are met, the maximum protection would be higher than in the current framework. However, in practice, the stringent wording and requirements for additional RDP mean the **current proposal reduces effective protection**, offering only an 8-year baseline (RDP + market protection) and a maximum of 9.5 years of effective protection in most cases. This will put Europe at a competitive disadvantage to attract global investments to innovate and unlock tomorrow's cures.

Linking incentives to access and continuous supply

The provision **conditioning RDP to the continuous supply of a medicine in all EU Member States within 2 years of granting the Marketing Authorization (MA) will not lead to more equitable patient access** for both current and future pipelines. Such a measure erroneously assumes that the industry has sole control over access and supply. In fact, this is fundamentally a shared responsibility with Member States and other external stakeholders. Some hurdles relate to the EU Member States' access ecosystem such as the requirement for external reference pricing (e.g. some require by law reimbursement in other countries before local submission[9]), the length of Health Technology Assessment or Pricing and Reimbursement (P&R) processes as well as differing evidence requirements, healthcare expenditure levels and priorities etc. For advanced therapies, which often rely on a limited number of specialized centers across the EU, it is not materially possible to launch and supply every country within 2 years. For vaccines, in over 50% of EU Member States, P&R processes cannot be triggered before the National Immunization Technical Advisory Groups' recommendation and further inclusion to a National Immunization Program – such processes can take several years[10]. There may also be challenges in the distribution chain that will prevent the industry, for reasons going beyond their sole control, to meet the supply conditionalities (e.g. terms and conditions or timing of tenders, unwarranted parallel trade). This **measure is therefore *de facto* not an incentive and it will not help overcome the multifactorial access hurdles** which are mostly within the P&R remits of EU Member States.

We do **share concerns regarding affordability and unequal access**, and medicines should reach all patients as quickly as possible after undertaking years of R&D. To address the multifactorial root causes of these disparities, we call for an evidence-based multistakeholder dialogue to devise solutions that address the challenges in the access ecosystem in a holistic manner. Taken together, we trust that these solutions can ultimately contribute to faster access for patients in Europe.

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[9] E.g. in GREECE a medicine needs to be reimbursed in at least 5 out of a basket of 11 reference countries specified by local law in order to fulfill local legal requirements to submit an application for reimbursement; in BULGARIA a drug needs to be reimbursed in at least 5 reference countries (out of 17); in HUNGARY a product needs reimbursement in at least 3 EU countries before local submission; in ROMANIA: we need to wait for HTA assessments (IQWIG,HAS,NICE, plus EUNETHTA – Romanian scorecard) and price publication in other countries (9+ sometimes 14+).

[10] Laigle, V. et al., Vaccine market access pathways in the EU27 and the United Kingdom, Vaccine 39 (2021)

Steering innovation in areas of (High) Unmet Medical Needs

Although the concept is embedded in a number of regulatory pathways (e.g. PRIME, conditional approval, accelerated assessment), we **understand efforts to better define what constitutes an Unmet Medical Need and call for clear and predictable criteria which reflect patient needs**. It is important to note however, that the nature and length of medicines' development is such that there are no certainties regarding whether a particular investment will ultimately be successful and address an UMN at the time of MA.

While we acknowledge the ambition to stimulate innovation for a subset of medicines which are expected to address an UMN (e.g. through meaningful reduction in morbidity and mortality), the definition of **UMN should not be too restrictive and reflect patient needs, such as significant improvements to their quality of life**. The definition should also account for the reality of science and be inclusive not only for breakthrough innovations, but also positive incremental developments. A more patient-centered definition would encourage research not only for life threatening or severely debilitating diseases, but also consider chronically debilitating diseases and those that significantly impact quality of life or contribute to patient care. The *risk* of high morbidity should also be factored into the definition to not only encourage research into treatments, but prevention and vaccines.